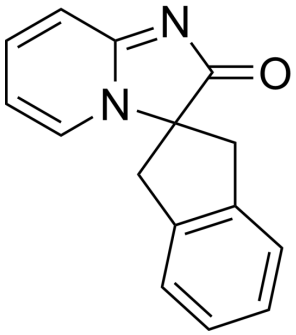
ZSET1446



Cat. No.:	HY-11013
CAS No.:	887603-94-3
Molecular Formula:	$C_{15}H_{12}N_2O$
Molecular Weight:	236
Target:	Calcium Channel; nAChR
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year

SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (211.86 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	4.2373 mL	21.1864 mL	42.3729 mL
	5 mM	0.8475 mL	4.2373 mL	8.4746 mL
	10 mM	0.4237 mL	2.1186 mL	4.2373 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (10.59 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (10.59 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (10.59 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

ZSET1446 is a novel cognitive enhancer that significantly improves learning deficits in various types of Alzheimer disease (AD) models.

In Vitro

ZSET1446 (100 pM-10 nM) exerts limited effects on the basal neuronal excitability and synaptic transmission. ZSET1446 potentiates the facilitatory effect of nAChR stimulation on sPSC frequency. ZSET1446 potentiates the increase in sIPSC frequency by local application of nicotine (5 μM; 2 minutes) without affecting the basal sIPSC frequency at the range of 10 pM to 1 nM[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

ZSET1446 enhances object recognition memory in mice and ameliorates cognitive impairment caused by scopolamine in rats. Concomitant administration of subeffective doses of ZSET1446 and memantine significantly ameliorates the cognitive performance in the novel object recognition task in both mice and rats. Moreover, oral administration of ZSET1446 or memantine increases the extracellular level of ACh in the hippocampus as compared with the control. Further, concomitant administration of subeffective doses of ZSET1446 and memantine significantly increases the extracellular level of ACh as compared with the group of ZSET1446 or memantine alone[2]. ZSET1446 (0.002, 0.01, and 0.1 mg/kg, p.o.) ameliorates cognitive deficits of SAMP8 after 4, 8, 12, and 16 weeks of treatment in a novel object recognition test. ZSET1446 also reduces grading scores of SAMP8 after 16 weeks of treatment. Further, 8-week treatment of ZSET1446 significantly reduces the total number of Aβ-positive granules in the hippocampus[3].

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PROTOCOL

Animal Administration [2]

The experimental apparatus consists of a Plexiglas open-field box [25 cm (width) × 41 cm (length) × 17 cm (depth), model TP-105], the floor of which is covered with sawdust. The apparatus is located in a sound-attenuated room. The procedure for the novel object recognition task consists of three different sessions: habituation, training, and retention sessions. Each mouse is individually habituated to the box, with 10 min of exploration in the absence of objects (day 1: habituation session). ZSET1446 at doses of 0.001, 0.003, 0.01, and 0.03 mg/kg and/or memantine at doses of 3 and 10 mg/kg is orally administered 60 min before the training trial. In the experiment of injection of nicotinic receptor antagonists, oral administration of ZSET1446 and i.p. injection of mechamylamine or DHbE at each dose of 1 mg/kg are given 60 min before the training trial. During the training session, two different novel objects are symmetrically fixed to the floor in the box, and each animal is allowed to explore in the box for 10 min (day 2: training session). These objects are different in shape and color but similar in size. The mice are considered to be exploring the object when the mouse is facing, touching, or sniffing the object. The time spent for exploring each object is manuallymeasured by a stopwatch. In the training session, locomotor activity is simultaneously measured for a period of 10 min automatically, using an Animex Auto placed under the open-field box. After the training trial, mice are immediately returned to their home cages.

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REFERENCES

[1]. Takeda K, et al. Potentiation of Acetylcholine-Mediated Facilitation of Inhibitory Synaptic Transmission by an Azaindolizione Derivative, ZSET1446 (ST101), in the Rat Hippocampus. J Pharmacol Exp Ther. 2016 Feb;356(2):445-55

[2]. Yamaguchi Y, et al. Combination effects of ZSET1446/ST101 with memantine on cognitive function and extracellular acetylcholine in the hippocampus. J Pharmacol Sci. 2013;123(4):347-55. Epub 2013 Nov 29.

[3]. Yamaguchi Y, et al. Effects of ZSET1446/ST101 on cognitive deficits and amyloid β deposition in the senescence accelerated prone mouse brain. J Pharmacol Sci. 2012;119(2):160-6.

Caution: Product has not been fully validated for medical applications. For research use only.

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